CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-452

MICROBIOLOGY REVIEW

Product Quality Microbiology Review
Review for HFD-150

26 MAR 2003

NDA: 20-452

Drug Product Name
Proprietary: Paraplatin
Non-proprietary: Carboplatin solution
Drug Product Classification: Anti-neoplastic

Review Number: 2

Subject of this Review
Submission Date: 11 OCT 2002
Receipt Date: 15 Oct 2002
Consult Date: 08 JAN 2003
Date Assigned for Review: 17 JAN 2003

Submission History (for amendments only)
Date(s) of Previous Submission(s): 31 MAR 1994
Date(s) of Previous Micro Review(s): 4 OCT 1994

Applicant/Sponsor
Name: Bristol-Myers Squibb
Address: P.O. Box 5400
Princeton, NJ 08543-5400
Representative: Noemi C. Guma, Ph.D.
Telephone: (609) 818-5759

Name of Reviewer: David Hussong

Conclusion: APPROVE

Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUPPLEMENT:** New NDA amendment

2. **SUPPLEMENT PROVIDES FOR:** Response to deficiencies in review dated 4 October 1994

3. **MANUFACTURING SITE:** Bristol Caribbean, Inc.
Mayaguez, PR 00708

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** 10 mg/mL solution of 10, 15 and 45 mL volumes in vials containing 50, 150 and 450 mg. The 50 mg product is in a — vial. The 150 mg product is in a —— vial. The 450 mg product is in a —— vial.

5. **METHOD(S) OF STERILIZATION:** ————

6. **PHARMACOLOGICAL CATEGORY:** Anti-neoplastic, cytotoxic

B. **SUPPORTING/RELATED DOCUMENTS:** DMF —— (datE of update is 3 June 1997).

C. **REMARKS:** This amendment responds to review comments from 1994. The original NDA described the aqueous form of a lyophilized product (NDA 19-880). The review of the original NDA noted that these were minor deficiencies and could be addressed as Phase 4 commitments.

The questions shown in the amendment are different from the questions sent in the review. It is not clear where they were altered.

filename: 20-452Rv2.doc

Executive Summary

I. **Recommendations**

A. **Recommendation on Approvability** - APPROVE

B. **Recommendations on Phase 4 Commitments and/or Agreements, if Approvable** – N/A

II. **Summary of Microbiology Assessments**

A. **Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology** – N/A

B. **Brief Description of Microbiology Deficiencies** – N/A

C. **Assessment of Risk Due to Microbiology Deficiencies** – N/A

III. **Administrative**

A. **Reviewer's Signature** _____

B. **Endorsement Block**
David Hussong/Microbiologist
Peter Cooney/Microbiology Supervisor

C. **CC Block**
cc:
Original NDA 20-452
HFD- 150/Division File/NDA 20-452

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/s/

David Hussong
3/27/03 10:13:09 AM
MICROBIOLOGIST

Peter Cooney
3/27/03 11:08:35 AM
MICROBIOLOGIST

CONSULTATIVE REVIEW TO HFD-150

OCT 5 1994

DIVISION OF MEDICAL IMAGING, SURGICAL, and DENTAL DRUG PRODUCTS; HFD-160

Microbiologist's Review #1
4 October 1994

A. 1. NDA 20-452

APPLICANT

Bristol-Myers Squibb Co.
Pharmaceutical Research Institute
5 Research Parkway
P.O. Box 5100
Wallingford, CT 06492-7660

2. PRODUCT NAMES: Paraplatin® — Carboplatin —

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: A 10 mg/mL solution of 10, 15 and 45 cc volumes in vial presentations containing 50, 150 and 450 mg (respectively) for dilution into a parenteral fluid and intravenous infusion over a 6 to 8 hour period. Dose rates are based on patient surface area.

4. METHOD(S) OF STERILIZATION: [redacted]

5. PHARMACOLOGICAL CATEGORY: Anti-neoplastic

6. DRUG PRIORITY CLASSIFICATION: 3P

B. 1. DATE OF INITIAL SUBMISSION: 31 March 1994

2. DATE OF AMENDMENTS: 31 March 1994 and 7 April 1994

3. RELATED DOCUMENTS: NDA 19-880, Paraplatin for Injection (lyophilized) and its Microbiologist's Reviews dates 27 February 1988 and 27 January 1989.

C. REMARKS: The product represents an aqueous presentation of the same drug for a lyophilized dosage form (NDA 19-880, approved 3 March 89). The original submission for NDA 19-880 [redacted] Also manufactured on these filling lines is Taxol (NDA 20-262) which was reviewed in December 1992 (Microbiologist's Review #1) and August 1993 (Microbiologist's Review #2). The lyophilized product contains equal quantities (w/w) of mannitol to drug substance, whereas the aqueous product contains only drug substance and water.

The 2 volumes of Amendment 1 contain a summary and 6 Attachments. These address [redacted] of stoppers and vials, [redacted] of filling equipment, and media fills.

D. CONCLUSIONS: The submission is not recommended for approval. However, issues described in the Microbiologist's Letter to the Applicant may be addressed post-approval, pending a commitment by the applicant. For additional details, refer to section "E. Review Notes".

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David Hussong, Ph.D.

cc:

Original NDA 20-452
HFD 160/Consult File
HFD 150/Division File
HFD 150/CSO/D.Daproza
HFD 150/Chemist/E.Tolgyesi
drafted by: D.Hussong, 10/04/94
R/D initialed by: P.Cooney, 10/05/94

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